Remarks

Reconsideration and withdrawal of the Examiner's rejections are requested respectfully.

Status of the Claims

The Examiner's Action addressed all pending claims, namely Claims 1 to 5 and 20 to 40. Claims 1 and 24 have been amended. Claims 41 to 53 have been added. Claim 21 has been cancelled. Accordingly, Claims 1 to 5, 20, and 22 to 53 are presented for the Examiner's consideration.

Support for the amendments to Claim 1 appears in the specification on page 1, lines 12 to 13.

Support for the newly added claims appears in the specification on page 4, lines 15 to 16, page 8, lines 20 to 22, page 9, lines 20 to 22, page 10, lines 16 and 17, page 13, lines 22 to 25, and page 22, lines 6 to 9.

Dependent Claim 24 has been indicated as allowable if rewritten in independent form to include the subject matter of base Claim 1. Claim 24 has been so amended.

Summary of the Examiner's Rejections

Claims 1 to 5, 21, 23, 25 and 28 to 39 have been rejected as being anticipated under 35 U.S.C. § 102(b) by European published application No. EP 797 991 (the Sherman reference).

Claims 1 to 5, 21, 23, 25 and 28 to 39 have been rejected as being anticipated under 35 U.S.C. § 102(e) by U.S. Patent No. 5,958,458 to Norling et al (the Norling reference).

Claims 1 to 5, 20 to 23, 25 and 30 to 40 have been rejected under 35 U.S.C. § 103(a) as being unpatentable on the basis of the disclosure of the Sherman reference in view of that of U.S. Patent No. 4,851,228 to Zentner et al. (the Zentner reference).

Claims 1 to 5, 20 to 23 and 25 to 40 have been rejected under 35 U.S.C. § 103(a) as being unpatentable on the basis of the disclosure of the Sherman reference in view of that of U.S. Patent No. 6,183,780 to Van Balken et al. (the Van Balken reference).

Claims 1 to 5, 20 to 23 and 25 to 40 have been rejected under 35 U.S.C. § 103(a) as being unpatentable on the basis of the disclosure of the Norling reference in view of that of the Van Balken reference.

Summary of Applicants' Invention

Applicants' invention relates to a pharmaceutical formulation which can be used for the treatment of depression or obsessive compulsive disorder. According to an aspect of the invention, the formulation for oral administration comprises: 1) particles of selective serotonin reuptake inhibitor (SSRI) or a pharmaceutically acceptable salt thereof, which particles are 2) coated with a rate-controlling polymer which allows controlled release of an SSRI over a period of not less than about 12 hours following oral administration. Fluvoxamine is an example of an SSRI.

The SSRI particles of the formulation may take the form of pellets or beads which compromise a core. The core may also comprise an organic acid. The core is coated with a rate-controlling polymer which forms a rate-controlling membrane surrounding the core. The rate-controlling membrane is effective in providing controlled release of an SSRI over a period of not less than about 12 hours following oral administration. Such controlled release enables an individual to use satisfactorily the formulation by ingesting it, for example, but once or twice daily.

In one embodiment of the invention, the rate-controlling membrane which coats the SSRI particles comprises a pharmaceutically acceptable film-forming, water-insoluble polymer. In another embodiment of the invention, the rate-controlling membrane may also comprise a mixture of the aforementioned water-insoluble polymer and a pharmaceutically acceptable film-forming, water-soluble polymer component.

The discussion which follows demonstrates that the disclosures of the cited references, either individually or in combination, do not anticipate or render obvious the present invention. A summary of each reference and of the Examiner's rejections appears below.

Summary of the References

The references cited by the Examiner in support of the §§ 102 and 103 rejections are summarized below.

European Patent Publication 0 797 991 A1 to Sherman

The Sherman reference discloses an extended release formulation containing venlafaxine hydrochloride which is referred to in the present application on page 5, 2nd and 3rd paragraphs, as an SSRI. The formulation is provided in the form of coated beads or spheroids and comprises an admixture of venlafaxine, microcrystalline cellulose, and hydroxypropylmethylcellulose (HPMC). The beads or spheroids are coated with a composition comprising ethyl cellulose and HPMC; they can be contained in a hard gelatin capsule for administration. The patent discloses that the dissolution rate for a single dose of the formulation provides a therapeutic blood serum level over a twenty-four hour period.

The only antidepressant disclosed in the Sherman reference is venlafaxine hydrochoride.

U.S. Patent No. 5,958,458 to Norling et al.

The Norling reference discloses a pharmaceutical particulate formulation in the form of cores, for example, pellets. The formulation comprises an active substance and a pharmaceutically acceptable inert carrier, for example, calcium carbonate. The cores may be coated or uncoated and compressed into the form of a tablet. The heart of the development described in this reference is the inert carrier which has certain specific properties, as described in Column 2, lines 22 to 32 of the patent.

The patent discloses that the invention described therein can be used with any number of active substances and lists about 30 classes of active substances and various compounds within the classes. Among this listing is general reference to anti-

depressants, including specifically imipramine, nortriptyline, and pritiptylene [sic] (protriptylene). There is no disclosure in the Norling patent concerning the coating of cores to provide a specified release profile of the antidepressant.

U.S. Patent No. 4,851,228 to Zentner

The disclosure of the Zentner patent is summarized in applicants' Reply, dated January 15, 2003, pages 6 and 7. The Examiner's Action indicates that the Zentner patent is relied upon solely for its disclosure that fluvoxamine is known to be an antidepressant (see the Examiner's Action, page 6, 1st paragraph, last line; see also the present application, page 1, 2nd paragraph).

U.S. Patent No. 6,183,780 to Van Balken et al.

The Van Balkan reference discloses an oral delayed/immediate release formulation comprising a compressed core which contains one or more active substances and which is surrounded with a coating. Various active substances are disclosed, including the antidepressant fluvoxamine. The coating contains one or more water-insoluble polymeric materials, for example, ethylcellulose, other water-insoluble cellulose derivatives, and polymethacrylates. There is no disclosure in the Van Balkan reference concerning the coating of cores which include an antidepressant to provide a specified release profile of the antidepressant.

Discussion of the Examiner's Rejections

Each of the Examiner's rejections is discussed hereafter.

The §102 Rejections Based on
the Sherman Reference and on the Norling Reference

Amended Claim 1 distinguishes over each of the Sherman and Norling disclosures in reciting, as an SSRI, fluoxetine, fluvoxamine, paroxetine, and sertraline. Neither the Sherman reference nor the Norling reference discloses any of these materials. Accordingly, withdrawal of the §102 rejections is requested respectfully.

The §103 Rejection Based on the Sherman and Zentner References

As discussed above, Claim 1 distinguishes over the disclosure of the Sherman reference in reciting a multiparticulate controlled release SSRI formulation which comprises particles of an SSRI selected from the group consisting of fluoxetine, fluvoxamine, paroxetine, and sertraline.

The Zentner reference discloses a composition which is referred to as a "multiparticulate osmotic pump". Although fluvoxamine is disclosed in a lengthy list of drugs for possible use in the pump, none of the examples discloses the use of fluvoxamine in particulate form coated with a rate-controlling polymer as claimed.

It is submitted respectfully that neither reference contains a disclosure which would provide one skilled in the art with the motivation to make the substitution proposed by the Examiner. Furthermore, there is no disclosure in either of the references that would lead one skilled in the art to conclude that applicants' compositions would provide

the release characteristics set forth in applicants' claims. Accordingly, reconsideration and withdrawal of this §103 rejection are requested respectfully.

The §103 Rejection Based on the Sherman and Van Balkan References

As discussed above, Claim 1 distinguishes over the disclosure of the Sherman reference in reciting a multiparticulate controlled release SSRI formulation which comprises particles of an SSRI selected from the group consisting of fluoxetine, fluvoxamine, paroxetine, and sertraline.

The heart of the development described in the Van Balkan patent is the provision of a coating which "ruptures".

It is submitted respectfully that neither reference contains a disclosure which would provide one skilled in the art with the motivation to make the substitution proposed by the Examiner. Furthermore, there is no disclosure in either of the references that would lead one skilled in the art to conclude that applicants' compositions would provide the release characteristics set forth in applicants' claims. Accordingly, reconsideration and withdrawal of this §103 rejection are requested respectfully.

The §103 Rejection Based on the Norling and Van Balkan References

Claim 1 distinguishes over the disclosure of the Norling reference in reciting a multiparticulate controlled release SSRI formulation which comprises particles of an SSRI selected from the group consisting of fluoxetine, fluvosamine, paroxetine, and sertraline. As mentioned above, the Norling reference discloses the antidepressants imipramine, nortriptyline and pritiptylene [sic] (protryptylene), but it fails to disclose the

antidepressants recited in Claim 1. Neither of these references discloses a formulation which has specified release properties, as set forth in applicants' claims. Accordingly, the combined disclosures of these two references would not lead to applicants' formulation. Reconsideration and withdrawal of the rejection are requested respectfully.

Added Claims 41 to 53

Added Claims 41 to 44 inclusive are dependent on "allowable" Claim 24 and individually recite one of the SSRI's that are referred to in Claim 1. Added Claim 45 is a method of treatment claim patterned after previously presented Claim 33, but dependent on Claim 24. Added Claim 46 defines the claimed formulation as being in tablet form.

Added Claim 47 and the claims dependent directly or indirectly thereon (Claims 48 to 53) define the rate-controlling polymer as being a polymeric acrylate or methacrylate lacquer substance as described in the present application on page 9, last two paragraphs.

It is submitted respectfully that the added claims are patentable also.

In view of the above, it is requested respectfully that the application be allowed in an early and favorable Action.

This Reply is accompanied by a Petition to extend the time to reply to the Office Action.

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